UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte PREETI LAL, JENNIFER L. HILLMAN, OLGA BANDMAN, PURVI SHAH, JANICE AU-YOUNG, HENRY YUE, KARL J. GUEGLER, and NEIL C. CORLEY

Appeal No. 2005-0102
Application No. 09/840,787

ON BRIEF

Before SCHEINER, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims related to a polynucleotide encoding a specified amino acid sequence. The examiner has rejected the claims for lack of patentable utility. We have jurisdiction under 35 U.S.C. § 134. We affirm.

Background

The specification discloses forty-nine proteins, generically referred to as "human regulatory molecules" or HRMs. The proteins were apparently identified as HRMs based on the presence of one of several structural motifs. See the specification, pages 2-4. Of particular interest in this appeal is the protein designated HRM-19, which has

the amino acid sequence shown in the specification's SEQ ID NO:19. See page 18. The specification discloses that "HRM-19 is 351 amino acids in length and has . . . one potential mitochondrial carrier motif, P_{31}LDVVKVRL. HRM-19 has sequence homology with C. elegans C16C10 (g577542) and is found in cDNA libraries associated with cell proliferation, cancer and immune response." Id.

The specification does not disclose any specific activity or function possessed by either HRM-19 or proteins having mitochondrial carrier motifs. Regarding "human regulatory molecules" generally, the specification discloses that

> [r]egulatory protein molecules function to control gene expression. These molecules turn individual or groups of genes on and off in response to various inductive mechanisms of the cell or organism; act as transcription factors by determining whether or not transcription is initiated, enhanced, or repressed; and splice transcripts as dictated in a particular cell or tissue.

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The specification discloses that HRMs are useful in therapy, particularly for cancers:

> In one embodiment, where HRM is an inhibitor, HRM . . . may be administered to a subject to treat a cancer such as adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, and terato-carcinoma. Such cancers include, but are not limited to, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus.
> . . .
> In a further embodiment where HRM is promoting cell proliferation, antagonists which decrease the expression or activity of HRM may be administered to treat a cancer such as adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, and teratocarcinoma. Such cancers include, but are not limited to, cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, muscle, ovary, pancreas,

> parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus.

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> In addition to therapy, the specification states that
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> [p]olynucleotides encoding HRM may be used for the diagnosis of conditions, disorders, or diseases which are associated with either increased or decreased expression of HRM. Examples of such conditions or diseases include adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and cancers of the adrenal gland, bladder, bone, brain, breast, cervix, gall bladder, ganglia, gastrointestinal tract, heart, kidney, liver, lung, bone marrow, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, and uterus; and immune disorders such as AIDS, Addison's disease, adult respiratory distress syndrome, allergies, anemia, asthma, atherosclerosis, bronchitis, cholecystit[i]s, Crohn's disease, ulcerative colitis, atopic dermatitis, dermatomyositis, diabetes mellitus, emphysema, atrophic gastritis, glomerulonephritis, gout, Graves' disease, hypereosinophilia, irritable bowel syndrome, lupus erythematosus, multiple sclerosis, myasthenia gravis, myocardial or pericardial inflammation, osteoarthritis, osteoporosis, pancreatitis, polymyositis, rheumatoid arthritis, scleroderma, Sjögren's syndrome, and thyroiditis.

Pages 47-48.

Discussion

1. Claim construction

Claims 2-14 and 21 are pending and on appeal. The claims stand or fall together. Appeal Brief, page 3. We will focus on claim 2, which reads as follows:

> 2. An isolated polynucleotide comprising a nucleic acid sequence encoding a protein having the amino acid sequence of SEQ ID NO:19 or the complete complement of the polynucleotide.

Thus, claim 2 is directed to a polynucleotide (RNA or DNA) that comprises a nucleotide sequence encoding the amino acid sequence shown in the specification's SEQ ID NO:19, or a complete complement of such a polynucleotide.

2. Utility

The examiner rejected claims 2-14 and 21 under 35 U.S.C. §§ 101 and 112, first paragraph, for lack of patentable utility.

The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. See In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility.").

The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement in the context of a claim to DNA. See In re Fisher, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005). The Fisher court interpreted Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966), as rejecting a "de minimis view of utility." 421 F.3d at 1370, 76 USPQ2d at 1229. The Fisher court held that § 101 requires a utility that is both substantial and specific. Id. at 1371, 76 USPQ2d at 1229. The court held that disclosing a substantial utility means "show[ing] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public." Id., 76 USPQ2d at 1230.

The court held that a specific utility is "a use which is not so vague as to be meaningless." Id. In other words, "in addition to providing a 'substantial' utility, an

asserted use must show that that claimed invention can be used to provide a well-defined and particular benefit to the public." Id.

The Fisher court held that none of the uses asserted by the applicant in that case were either substantial or specific. The uses were not substantial because "all of Fisher's asserted uses represent merely hypothetical possibilities, objectives which the claimed ESTs, or any EST for that matter, could possibly achieve, but none for which they have been used in the real world." Id. at 1373, 76 USPQ2d at 1231. "Consequently, because Fisher failed to prove that its claimed ESTs can be successfully used in the seven ways disclosed in the '643 application, we have no choice but to conclude that the claimed ESTs do not have a 'substantial' utility under § 101." Id. at 1374, 76 USPQ2d at 1232.

"Furthermore, Fisher's seven asserted uses are plainly not 'specific.' Any EST transcribed from any gene in the maize genome has the potential to perform any one of the alleged uses. . . . Nothing about Fisher's seven alleged uses set the five claimed ESTs apart from the more than 32,000 ESTs disclosed in the '643 application or indeed from any EST derived from any organism. Accordingly, we conclude that Fisher has only disclosed general uses for its claimed ESTs, not specific ones that satisfy § 101." Id.

In this case, the examiner found that "the specification does not assert any specific utility for HRM-19 and provides no additional evidence that HRM-19 has any specific function. . . . There is no teaching of any specific diseases or conditions associated specifically with HRM-19." Examiner's Answer, page 4.

The examiner noted that the specification discloses that HRM-19 has a mitochondrial carrier motif, but concluded that this property does not suggest a patentable utility:

> Even if this protein is a mitochondrial carrier protein, one of ordinary skill in the art would not know which compound is a substrate for the carrier. Humans produce many mitochondrial carriers and each mitochondrial carrier is expected to have a specific substrate(s) and function that cannot be predicted based on sequence homology alone. The art teaches that there are many mitochondrial carriers that import various metabolites, nucleotides, cofactors and compounds which are not synthesized in mitochondria.

Examiner's Answer, page 5 (citing Palmieri, "Mitochondrial carrier proteins," FEBS Letters, Vol. 346, pp. 48-54 (1994), of record).

The examiner also noted that the specification discloses that HRM-19 is similar to a protein from C. elegans but concluded that this, too, failed to suggest a patentable utility, because "[t]he sequence search performed by US PTO shows that SEQ ID NO:19 has about 35% homology with C. elegans C16C10 that is defined by GenBank as 'similar to carrier protein', i.e. similar to a protein for which the function is not established." Examiner's Answer, page 5. The examiner concluded that "a protein of SEQ ID NO:19 is an uncharacterized protein with no known specific function." Id., page 6.

With respect to the specification's disclosure that polynucleotides encoding SEQ ID NO:19 can be used to detect the level of expression of the corresponding gene, the examiner noted that "for a method of detection of a nucleic acid in a sample to be useful, one must know the biological significance of the polypeptide(s) which is(are) being detected. Without this information, the results of the expression profile are useless because one would not know . . . what significance could be attributed to such changes in expression profiles. Without this knowledge, which could not be gleaned from the instant specification as filed, one of ordinary skill in the art at the time the

instant invention was made would not have been able to use the information obtained from an expression profile in a useful manner." Examiner's Answer, page 6.

The examiner noted that claims 13, 14, and 21 are directed to diagnostic methods but noted that "[n]either the specification nor the art of record disclose any specific disease or conditions that can be diagnosed using a DNA encoding SEQ ID NO:19. There is no indication that increasing or decreasing the expression of HRM-19 would have any use in diagnosing any diseases. . . . There is no motivation to specifically select lung tissue an[d] lung cancer as a tissue and disease from the non-discriminatory list of cancers of various types an[d] tissues disclosed on page 47, lines 24-29 of the specification." Examiner's Answer, page 7.

We agree with the examiner that the specification fails to disclose a utility that satisfies the requirements of 35 U.S.C. § 101. Appellants argue that the claimed polynucleotides are useful because they can be used in expression profiling methods in connection with "toxicology testing, drug discovery, and disease diagnosis." See the Appeal Brief, pages 7-15. According to Appellants, "all expressed genes have a utility for toxicological screening," and therefore so does SEQ ID NO:19. See id., page 14.

A utility that could be asserted for any expressed human gene is not a "specific" utility that will satisfy § 101. See Fisher, 421 F.3d at 1370, 76 USPQ2d at 1230 (a specific utility requires "that [the] claimed invention can be used to provide a well-defined and particular benefit to the public") and id. at 1374, 76 USPQ2d at 1232 ("Any EST transcribed from any gene in the maize genome has the potential to perform any one of the alleged uses. . . . Nothing about Fisher's seven alleged uses set the five claimed ESTs apart from the more than 32,000 ESTs disclosed in the '643 application or indeed

from any EST derived from any organism. Accordingly, we conclude that Fisher has only disclosed general uses for its claimed ESTs, not specific ones that satisfy § 101").

As Appellants themselves have asserted, any expressed human gene could be used to carry out expression profiling. Therefore, that potential use is not specific to the claimed polynucleotides and does not meet the requirements of § 101.

In view of the disclosure of the instant case, that potential use is also not substantial. As the examiner has pointed out, the specification provides no guidance on the meaning of a change in HRM-19 expression. A substantial utility is one that makes the invention useful to the public in its current form, not potentially useful in the future after further research. See Fisher, 421 F.3d at 1371, 76 USPQ2d at 1230. Since the specification does not provide a disclosure that would allow those skilled in the art to use the information that results from an expression profiling experiment in any practical way, expression profiling of HRM-19 is not a substantial utility that would satisfy § 101.

Appellants also assert that HRM-19 is useful because it is likely to be a mitochondrial carrier protein. See the Appeal Brief, page 15: "[T]he polypeptide encoded for by the claimed polynucleotide shares more than 35% amino acid sequence identity over 351 amino acid residues with C. elegans C16C10 (g577542) . . . , a putative mitochondrial carrier protein. . . . This is more than enough homology to demonstrate a reasonable probability that the utility of the mitochondrial carrier protein family can be imputed to the claimed invention (through the polypeptide it encodes)."

We do not find this argument persuasive, because nowhere in the specification or the Appeal Brief do Appellants explain what "utility" is possessed by members of "the mitochondrial carrier protein family" and thereby imputed to HRM-19. Appellants assert

that "the mitochondrial carrier family of proteins includes carriers involved in the transport of ions and charged metabolites between the cytosol and the mitochondrial matrix." Appeal Brief, page 15. We can assume, for the sake of argument, that Appellants are correct in asserting that HRM-19 is likely to be a mitochondrial carrier protein.[1]

That assertion, however, does not establish the patentable utility of the claimed polynucleotides, because Appellants do not explain what utility is shared by mitochondrial carrier proteins. That is, assuming that HRM-19 is a mitochondrial carrier protein that is involved in transporting ions and charged metabolites between the cytosol and the mitochondrial matrix, how does that make it useful to a person of skill in the art? Appellants provide no answer to this question and none is apparent to us from the evidence of record.[2] Therefore, we find that classifying a protein as a mitochondrial carrier protein does not, by itself, disclose a specific and substantial utility to those skilled in the art.

Finally, Appellants assert that "[t]he Lal declaration clearly demonstrates that the transcripts for HRM-19 were significantly, differentially, up-regulated (overexpressed) in lung tissue samples from cancer patients as compared to matched normal samples from the same patient. Therefore, HRM-19, and the cDNA encoding it, are of diagnostic use in detecting lung cancers." Appeal Brief, pages 17-18. Appellants also assert that "[t]he use of polynucleotides encoding HRM to detect cancer, and the association of increased

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[1] The examiner disputes this assertion, but we need not resolve the dispute in this case.
[2] We have not considered the Yu et al. reference cited on page 16 of the Appeal Brief. That reference was published in 2001, while the instant application apparently has an effective filing date of September 23, 1997. "Enablement, or utility, is determined as of the application filing date." In re Brana, 51 F.3d 1560, 1567 n.19, 34 USPQ2d 1436, 1441 n.19 (Fed. Cir. 1995). Post-filing evidence can be considered only to the extent that it shows the state of the art as of the effective filing date. See In re Hogan, 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977) ("[U]se of later publications as evidence of the state of

amounts of transcript with cancer is further disclosed in the specification at, for example, p. 48, lines 7-16, and p. 48, line 29 through p. 49, line 1."

We agree with Appellants that overexpression of a particular DNA sequence in lung cancer cells (compared to noncancerous cells) is a utility that could satisfy the "specific and substantial" requirements of § 101. The problem here is that the specification does not disclose that HRM-19, as opposed to HRM-1 through HRM-18 or HRM-20 through HRM-49, is useful for diagnosing cancer of the lung, as opposed to any of the thirty-three other types of cancer or thirty-three immune disorders that are listed on pages 48-49 along with lung cancer.

Essentially, the specification discloses a set of forty-nine proteins, each of which is asserted to be useful in diagnosing or treating a set of sixty-seven diseases. According to Appellants, if any of these 3283 (49 x 67 = 3283) combinations turns out to be accurate, that is sufficient to support a patent.

We do not agree. The disclosure in the instant specification lacks the specificity required to say that it discloses, in the sense of § 112, first paragraph, that HRM-19 is useful in diagnosing lung cancer. True, the specification discloses forty-nine HRM proteins and sixty-seven different diseases; with hindsight, one can pick HRM-19 and lung cancer from the relevant groups and say that that combination is disclosed, together with 3282 others.

This kind of generic disclosure, however, has been held to be inadequate to support a claim to one particular species that is encompassed by the genus. For

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art existing on the filing date of an application" is acceptable). Appellants have not shown that Yu's disclosure is evidence of the state of the art as of Sept. 23, 1997; therefore, we have not considered it.

example, in In re Ruschig, the specification disclosed a genus of "something like half a million possible compounds," of which one was claimed. 379 F.2d 990, 993, 154 USPQ 118, 122 (CCPA 1967). The court held that specific claims to single compounds require some sort of "blaze marks" directing those skilled in the art to those particular compounds. See id. at 993, 154 USPQ at 122.

The court has since applied the Ruschig test to inventions other than chemical compounds. For example, in Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 56 USPQ2d 1481 (Fed. Cir. 2000), the invention was a method of treating pain by administering a dose of medicine that met specified pharmacokinetic parameters. The court held that the specified combination of parameters was not adequately disclosed: "As Ruschig makes clear, one cannot disclose a forest in the original application, and then later pick a tree out of the forest and say 'here is my invention.' In order to satisfy the written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure." Id. at 1326-27, 56 USPQ2d at 1486.

This case differs from Ruschig and Purdue Pharma in that there is no dispute that the particular compound of claim 2 is adequately described.[3] The same issue arises, however, in considering whether the use of that compound in diagnosing lung cancer is disclosed adequately in the specification, such that the Lal declaration could be considered to support a disclosed utility, or whether the specification's disclosure is so inadequate that the utility must be considered to be disclosed for the first time in the declaration.

[3] We have some doubts, however, about whether claims 14 and 21 are adequately described. If this application is subject to further prosecution, the examiner should consider whether claims 14 and 21, as

We conclude that the specification does not provide blaze marks that would lead a person of skill in the art to the specific combination of HRM-19 and diagnosis of lung cancer. The specification provides only a single list of sixty-seven diseases, which are said to be applicable to all of the forty-nine disclosed HRMs. The specification provides no further details on which HRMs are expected to be associated with which diseases. Thus, the specification provides none of the blaze marks that the Ruschig court held to be necessary to specifically describe a species encompassed by a disclosed genus.

Therefore, Appellants' generic disclosure lacks the specificity necessary to consider it to describe using HRM-19 to diagnose lung cancer. Rather, that disclosure is made for the first time in the Lal declaration. Because the specification does not adequately disclose that HRM-19 is useful for diagnosing lung cancer, the post-filing evidence presented in the Lal declaration does not support a disclosed utility and cannot be relied upon to establish that HRM-19 has patentable utility. See In re Brana, 51 F.3d 1560, 1567 n.19, 34 USPQ2d 1436, 1441 n.19 (Fed. Cir. 1995) (A post-filing declaration cannot be used to "render an insufficient disclosure enabling," but only "to prove that the disclosure was in fact enabling when filed (i.e., demonstrat[ing] utility).").

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amended, are adequately described by the originally filed specification, under the test set out in In re Ruschig.

Summary

The specification does not disclose a specific and substantial utility for the claimed polynucleotides. The post-filing evidence presented in the Lal declaration cannot be relied on because the specification does not adequately describe the utility to which the Lal declaration is directed. We therefore affirm the rejection of claim 2 under 35 U.S.C. §§ 101 and 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

Toni R. Scheiner)
Administrative Patent Judge)
)
)
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)
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Eric Grimes)
Administrative Patent Judge)

EG/jlb

Foley & Lardner
Suite 500
3000 K Street, NW
Washington, DC 20007